

**REMARKS**

Claims 1-35 were pending in the instant application as of the issuance of the Office Action mailed on July 14, 2005. According to the foregoing amendments, claims 1-35 are cancelled without prejudice to the prosecution of these claims in this or a subsequently filed application. New claims 36-59 are filed herein. Support for these new claims can be found throughout the specification and in the claims as originally filed, for example, claims 1-5, 11-15 and 21-24 as originally filed. No new matter is introduced by these amendments.

***Sequence Compliance***

In accordance with the Examiner's suggestion, Applicants have amended the specification by the foregoing amendments to indicate that the amino acid sequence (*i.e.*, residues 1-610) as set forth in Table 9 corresponds to SEQ ID NO:1.

***Restriction Requirement***

Claims 1-35 are subject to a restriction requirement under 35 U.S.C. 121 and 372. The Examiner has required restriction between the following inventions in the above-identified application:

Group I: Claims 1-5, 9-10 and 35, drawn to isolated proteins comprising at least a subsequence of the amino acid sequence of LTA<sub>4</sub> hydrolase as disclosed in Table 9;

Group II: Claims 6-8 and 25, drawn to compounds that are complementary to the LTA<sub>4</sub> hydrolase described in Table 9;

Group III: Claims 11-15, drawn to methods of using the parameter of the protein described in Table 9 (LTA<sub>4</sub> hydrolase) in drug design;

Group IV: Claims 11-15, drawn to methods of using the parameters of the compound complementary to the protein described in Table 9 (LTA<sub>4</sub> hydrolase) in drug design;

Group V: Claims 16-18, drawn to methods for screening LTA<sub>4</sub> hydrolase analogues;

Group VI: Claims 19-20, 30-31 and 35, drawn to analogues of LTA<sub>4</sub> hydrolase;

Group VII: Claims 21-24, drawn to methods of screening compounds that are complementary to LTA<sub>4</sub> hydrolase described by Table 9;

Group VIII: Claims 26-27, drawn to methods of engineering a protein that is an analogue of LTA<sub>4</sub> hydrolase;

Group IX: Claim 28, drawn to processes of purifying an LTA<sub>4</sub> hydrolase as set forth in Table 9;

Group X: Claim 28, drawn to processes of purifying an LTA<sub>4</sub> hydrolase analogue;

Group XI: Claim 29, drawn to methods of crystallization of an LTA<sub>4</sub> hydrolase;

Group XII: Claims 32-33, drawn to nucleic acids encoding LTA<sub>4</sub> hydrolase analogues; and

Group XIII: Claim 34, drawn to use of LTA<sub>4</sub> hydrolase analogues in the preparation of LTB<sub>4</sub> or other metabolites in the leukotriene cascade.

Applicants' respectfully traverse the foregoing Restriction Requirement and submit that the requirement is improper. However, in order to be considered responsive to the instant Office Action, Applicants' hereby elect Group III (claims 11-15) drawn to methods of using the parameters of the protein described in Table 9 (LTA<sub>4</sub> hydrolase) in drug design, *with traverse*. Applicants note that new claims 36-48 are directed to drug design and fall under Group III. Applicants traverse the restriction requirement to the extent that Groups III and VII should be reformed as a single group containing new claims 36-59 (claims 36-48 falling under Group III and claims 49-59 falling under Group VII).

In requiring restriction, the Examiner states

The human LTA<sub>4</sub> hydrolase purified by Minami *et al.* (1988) has an amino acid sequence which is identical to that in Table 9 of the instant application... The three dimensional form of a protein is an inherent property that [is] directly related to its amino acid sequence. Hence, the LTA<sub>4</sub> hydrolase taught by Minami *et al.* has both a subsequence of an LTA<sub>4</sub> hydrolase and the 3-D form essentially disclosed in Table 9. Thus, the technical feature of Group I is not a special technical feature because it does not define a contribution that the Group makes over the prior art. Without a special technical feature, the pending claims are restricted according to their substance as different products (Groups I, II, VI, XII and XIII), and their different categories (Groups II-V and VII-XI, method claims). (Office Action, page 4)

Applicants respectfully disagree. Applicants assert that the present invention is based, in part, on the elucidation of the three dimensional structure of the LTA<sub>4</sub> hydrolase protein crystal, exclusively defined by the present invention. Applicants argue that despite the teachings of

Minami *et al.*, the prior art failed to teach or suggest the three dimensional structure of the protein. Moreover, the elucidation of the three dimensional structure of a protein is not a routine process, even given knowledge of the amino acid sequence of the protein. Indeed, the crystal structure was produced using specific optimized conditions, which would not have been obvious to one skilled in the art at the time of filing of the present application. As such, the characterization of the three dimensional structure of the LTA<sub>4</sub> hydrolase protein as taught exclusively by the present invention can be considered a special technical feature shared by the claims of the present invention and, in particular, the claims of Group III and VII.

In addition, a literature search of both Groups III and VII would be nearly, if not completely, co-extensive. Accordingly, Applicants respectfully submit that a sufficient search and examination with respect to the claimed methods can be made without serious burden on the Examiner. As the M.P.E.P. states:

[i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. M.P.E.P. § 803.

Indeed, Applicants submit that the search and examination of Groups III and VII would not place a serious burden on the Examiner, and therefore respectfully request withdrawal of the restriction of the two Groups.

#### ***Species Election***

The Examiner has further required a species election between (a) the general metallohydrolase inhibitor of claim 22, (b) the epoxide hydrolase inhibitor of claim 23 and (c) the antagonist of an LTB<sub>4</sub> receptor of claim 24. Accordingly, should the Examiner allow for search and examination of Groups III and VII, Applicants elect a compound which inhibits epoxide hydrolase and/or aminopeptidase activity of LTA<sub>4</sub> hydrolase or LTA<sub>4</sub> syntheses to which claim 48 (the claim readable on the elected species) shall be restricted, if the generic claim is deemed not allowable.

For at least each of the foregoing reasons, Applicants respectfully request that the restriction requirement be withdrawn, and that all of the claims presently pending in this application, *i.e.*, claims 38-59, be examined. Applicants reserve the right to traverse the restriction between the non-elected groups in this or a separate application.

Applicants believe that no fee is due with this statement. However, if a fee is due, please charge our Deposit Account No. 12-0080, under Order No. PVZ-006US from which the undersigned is authorized to draw.

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Respectfully submitted,

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